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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,952	06/15/2006	Yolande Rouiller	ARS-129	1577

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EXAMINER	
LANDSMAN, ROBERT S	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,952	ROUILLER, YOLANDE	
	Examiner	Art Unit	
	ROBERT LANDSMAN	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,20-26 and 30-32* is/are pending in the application.

4a) Of the above claim(s) *21 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,20,22,24-26 and 30-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Formal Matters

A. The Supplemental Amendment, filed 3/5/08 has been entered

B. The Amendment filed 2/25/08 has been entered.

C. Claims 17, 20-26 and 30-42 are pending. Claims 21 and 23 are withdrawn as discussed previously. Therefore, claims 17, 20, 22, 24-26 and 30-42 are the subject of this Office Action.

2. Claim Objections

A. All claim objections have been withdrawn in view of Applicants' arguments, or amendments to the claims.

3. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 17, 20, 22, 24-26 and 30-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing the recombinant TBP-1 of SEQ ID NO:1 in a CHO cell, does not reasonably provide enablement for a method of producing a mutein which is less than 100% identical to SEQ I D NO:1, or encoded by polynucleotides which hybridize to polynucleotides encoding SEQ ID NO:1, as well as for using all cells other than CHO cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to claiming methods of producing recombinant TBP-1 muteins which are less than 100% identical to SEQ I D NO:1, or encoded by polynucleotides which hybridize to polynucleotides encoding SEQ ID NO:1. These "**muteins**" and

polynucleotides which "**hybridize**" under moderate or stringent conditions to those encoding SEQ ID NO:1 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to said polynucleotides, or encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:1.

Applicants provide no guidance or working examples of nucleic acid molecules which hybridize to those encoding SEQ ID NO:1, or which are "**at least 40%" to "90%**" identical to SEQ ID NO:1, nor do they provide a *function* of these muteins. Furthermore, it is not predictable to one of ordinary skill in the art what the functions of these nucleic acids, or the proteins/muteins which they encode, are, nor how to make a functional TBP-1 which is less than 100**%** identical to SEQ ID NO:1

Furthermore, Applicants are only enabled for this method with the **use of CHO cells**. No other cell line has been shown to effectively produce high yield of TBP-1 protein at the claimed temperatures. Support for this state of the art is seen in Furukawa (Cytotechnology 1998 – reference R10 on the 1449 filed 6/15/06). Furukawa teach that the effect of temperature on protein production is cell dependent (Introduction).

In summary, the breadth of the claims is excessive with regard to Applicants claiming methods of producing recombinant TBP-1 muteins which are less than 100% identical to SEQ I D NO:1, or encoded by polynucleotides which hybridize to polynucleotides encoding SEQ ID NO:1 as well as the use of cell lines other than CHO cells. There is also a lack of guidance and working examples of these nucleic acid molecules and proteins/muteins. Applicants do not provide a function of these nucleic acid molecules, or a function of the proteins which they encode. These factors, along with the lack of predictability to one of ordinary skill in the art as to what the functions of these proteins/muteins are, or of how to make a functional TBP-1 less than the full length of SEQ ID NO:1, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

4. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 17, 20, 22, 24-26 and 30-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Muteins which are "**40%**" to "**90%**" identical to SEQ ID NO:1, or which "**hybridize**" to polynucleotides encoding SEQ ID NO:1, would have one or more nucleic acid

substitutions, deletions, insertions and/or additions to said polynucleotides. Similarly, these muteins would encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:1.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:1, or molecules which hybridize to the polynucleotides encoding this SEQ ID NO (which could be at least thousands of molecules), alone, are insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

Similarly, the genus of cells capable of performing the claimed method has not been adequately described. Applicants have only provided adequate written description that **CHO cells** are capable of producing an increase in TBP-1.

5. Claim Rejections - 35 USC § 112, second paragraph

A. All rejections under 35 USC 112, second paragraph, have been withdrawn in view of Applicants' arguments, or amendments to the claims.

B. Claims 20 is vague and indefinite since the claim recites "moderate" and "stringent conditions." It is not known what these conditions are. Nucleic acid molecules which hybridize under conditions of "low" stringency would not necessarily hybridize under conditions of "high" stringency. Furthermore, not all conditions of "high" or "low" stringency, for example, are the same. Therefore, it is required that Applicants amend the claims to recite the exact hybridization conditions without using indefinite phrases such as "*for example*" **without adding new matter**.

6. Claim Rejections - 35 USC § 102

A. The rejection of all claims under 35 USC 102 has been withdrawn in view of Applicants' arguments and amendments to the claims to limit the protein to TBP-1.

7. Claim Rejections - 35 USC § 103

A. The rejection of all claims under 35 USC 102 has been withdrawn in view of Applicants' arguments and amendments to the claims to limit the protein to TBP-1.

B. Claims 17, 20, 22, 24-26 and 30-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furukawa et al. (reference R11 on the 1449 submitted 6/15/06). The claims recite a method of producing TBP-1 by culturing cells between about 25 °C and 29 °C.

Furukawa teach a method of producing an increased yield of an enzyme by culturing CHO cells at 32 °C (Figures 1 and 2). In fact, Furukawa also teach that the production of another protein, FVIII, was increased at a temperature of 27 °C (Introduction). Furukawa teach the use of serum-free media (page 86, under "Cell line, maintenance and product").

Furukawa do not teach the production of TBP-1. However, it would have been obvious to have used any protein in the invention of Furukawa since it is desirable to increase protein yield for experimental or therapeutic use. This addresses "(1)" on page 9 of Applicants' Response to KSR on 2/25/08. The technique would have been identical to that of using the enzyme of Furukawa)

Furukawa teach using a temperature of 27°C (Introduction). Therefore, if Applicants argue that Furukawa, itself, does not use a temperature of below 32 °C, it still would have been obvious to try temperatures below 32 – at least to 27 °C since this has been shown to be successful. In addition, there are only a finite number of predictable potential solutions (the use of CHO cells, for one) to using temperatures in the range of about 27-32 °C. Not only is the temperature range small, but protein levels would only be expected to increase, decrease, or remain the same. This addresses "(2)" and "(3)" of Applicants' KSR argument.

Under *KSR*, it's now apparent "obvious to try" may be an appropriate test in more situations than we previously contemplated. When there is motivation to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was

obvious to try may show that it was obvious under § 103 (*KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007)).

8. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman, Ph.D. whose telephone number is (571) 272-0888. The examiner can normally be reached on M-F 10 AM – 6:30 PM (eastern).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Robert Landsman/
Primary Examiner, Art Unit 1647